REMARKS

The specification has been amended to correct truncated gene designations and include the Official Symbol for a particular gene designation. In particular, Table 4C has been amended to replace the inadvertently truncated gene designation "*inhibitor of kappa light polypeptide gene enhancer*", which is indicated as corresponding to the symbol "*IKBKAP*" in Table 4C, with the complete gene designation "*inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase complex-associated protein*". The designation "*inhibitor of kappa light polypeptide gene enhancer*" is an obvious inadvertent truncation of the designation "*inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase complex-associated protein*", since it is indicated as corresponding to the symbol "*IKBKAP*" in Table 4C, and since the designation "*inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase complex-associated protein*" is the Official Name of the gene for which the Official Symbol is "*IKBKAP*", as indicated in the attached "NCBI Gene database entry for IKBKAP" (Appendix E). Thus, this amendment does not introduce new matter into the specification.

Table 4D has been amended to replace the gene designation "*HSPCA*" with the gene designation "*HSP90AA1*", and to replace the gene designation "*heat shock 90kDa protein 1, alpha*" with the gene designation "*heat shock protein 90kDa alpha (cytosolic), class A member 1*". The gene designations "*heat shock protein 90kDa alpha (cytosolic), class A member 1*" and "*HSP90AA1*" are the current Official Name and Official Symbol, respectively, of the gene for which "*HSPCA*" and "*heat shock 90kDa protein 1, alpha*" are alternate designations, as indicated in the attached "NCBI Gene database entry for HSP90AA1" in the "Other Aliases" and "Other Designations" sections (Appendix F). Thus, this amendment does not introduce new matter into the specification.

In addition, Table 4D has been amended to replace the inadvertently truncated gene designation "*vmaf musculoaponeurotic fibrosarcoma oncogene homo*", which is indicated as corresponding to the gene designation "*MAFB*" in Table 4D, with the complete gene designation "*v-maf musculoaponeurotic fibrosarcoma oncogene homolog B (avian)*". The designation "*vmaf musculoaponeurotic fibrosarcoma oncogene homo*" is an obvious inadvertent truncation of the complete designation "*v-maf musculoaponeurotic fibrosarcoma oncogene homolog B (avian)*", since it is used to designate the gene "*MAFB*" in Table 4D and since "*v-maf musculoaponeurotic fibrosarcoma oncogene homolog B (avian)*" is the Official

Name of the gene for which the Official Symbol is "*MAFB*", as indicated in the attached "NCBI Gene database entry for MAFB" (Appendix G).

Paragraphs [0584], [0585] and [0586] of the publication of the application have been amended to replace the alternate gene designation "*HSPCA*" with the current Official Symbol "*HSP90AA1*". As discussed above, "*HSP90AA1*" are the current Official Symbol for "*HSPCA*". Thus, these amendments do not introduce new matter into the specification.

Claims 76 and 82 to 98 are pending in this application.[1] Claims 76, 83, 86, 87, 89, 92, 93, 95, and 98 have been amended. In particular, claims 76, 87 and 93 have been amended to replace "*HSPCA*" with the gene designation "*heat shock protein 90kDa alpha (cytosolic), class A member 1 (HSP90AA1)*". Table 4D (at row having "*211969_at*" as first column entry) indicates that the symbol "*HSPCA*" corresponds to the gene designation "*heat shock 90kDa protein 1, alpha*". As of the effective date of the application, "*HSPCA*" was known to be a symbol for the gene designation "*heat shock 90kDa protein 1, alpha*".

Claims 76, 87 and 93 have also been amended to indicate that "*IKBKAP*" is a symbol for the gene designation "*inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase complex-associated protein*". Table 4C (at row having "*ncr8843*" as first column entry) indicates that "*IKBKAP*" corresponds to the inadvertently truncated gene designation "*inhibitor of kappa light polypeptide gene enhancer*", which where the complete recitation of this truncated designation is "*inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase complex-associated protein*", as set forth in the present amendments to the specification. As of the effective date of the application, "*IKBKAP*" was known to be a symbol for the gene designation "*inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase complex-associated protein*".

Claims 76, 87 and 93 have also been amended to indicate that "*IL13RA1*" is a symbol for the gene designation "*interleukin 13 receptor, alpha 1*". Table 4C (at row having "*seob4945*" as first column entry) indicates that the gene designation "*interleukin 13 receptor, alpha 1*" corresponds to the symbol "*IL13RA1*". In addition, as of the effective date of the application, "*IL13RA1*" was known to be a symbol for the gene designation "*interleukin 13 receptor, alpha 1*".

Claims 76, 87 and 93 have also been amended to indicate that "*LAMC1*" is a symbol for the gene designation "*laminin, gamma 1*". Table 4C (at row having "*seoa0469*" as first column entry) indicates that the gene designation "*laminin, gamma 1*" corresponds to the

[1] Applicants note that the "Disposition of Claims" indicates that claim 76 to 98 are pending in this application. However, claims 77 to 81 were canceled in the Response To Restriction Requirement And Preliminary Amendment filed on February 1, 2010. Thus, claims 76 and 82 to 98 are pending and under examination in the present application.

symbol "*LAMC1*". In addition, as of the effective date of the application, "*LAMC1*" was known to be a symbol for the gene designation "*laminin, gamma 1*".

Claims 76, 87 and 93 have also been amended to indicate that "*MAFB*" is a symbol for the gene designation "*v-maf musculoaponeurotic fibrosarcoma oncogene homolog B (avian) (MAFB)*". Table 4D (at row having "*218559_x_at*" as first column entry) indicates that the symbol "*MAFB*" corresponds to the inadvertently truncated gene designation "*vmaf musculoaponeurotic fibrosarcoma oncogene homo*", where the complete recitation of this truncated designation is "*v-maf musculoaponeurotic fibrosarcoma oncogene homolog B (avian)*", as set forth in the present amendments to the specification. In addition, as of the effective date of the application, "*MAFB*" was known to be a symbol for the gene designation "*v-maf musculoaponeurotic fibrosarcoma oncogene homolog B (avian)*".

Claims 76, 87 and 93 have also been amended to indicate that "*PF4*" is a symbol for the gene designation "*platelet factor 4 (PF4)*". Table 1U (at row having "*206390_x_at*" as first column entry) indicates that the gene designation "*platelet factor 4*" corresponds to the symbol "*PF4*". In addition, as of the effective date of the application, "*PF4*" was known to be a symbol for the gene designation "*platelet factor 4 (PF4)*".

Claims 83, 86, 89, 92, 95, and 98 have been amended to replace the recitation "*wherein said classifier is identified as classifier 100000252*" with the recitation "*wherein said classifier has a format SCORE = –1.839 + 0.8*HSP90AA1 – 1.5525*IKBKAP + 1.10184*IL13RA1 + 0.78923*LAMC1 – 1.3974*MAFB + 1.0602*PF4, where*

SCORE, if positive, classifies said test subject into said class representing human subjects having mild osteoarthritis;

SCORE, if negative, classifies said test subject into said class representing human subjects not having osteoarthritis;

HSP90AA1 represents said level of expression of heat shock protein 90kDa alpha (cytosolic), class A member 1 (HSP90AA1) in said sample of said test subject;

IKBKAP represents said level of expression of inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase complex-associated protein (IKBKAP) in said sample of said test subject;

IL13RA1 represents said level of expression of interleukin 13 receptor, alpha 1 (IL13RA1) in said sample of said test subject;

LAMC1 represents said level of expression of laminin, gamma 1 (LAMC1) in said sample of said test subject;

MAFB represents said level of expression of v-maf musculoaponeurotic fibrosarcoma oncogene homolog B (MAFB) in said sample of said test subject; and PF4

represents said level of expression of platelet factor 4 (PF4) in said sample of said test subject".

Support for this amendment relating to classifier 100000252 ean be found in the published application at least Section 6.1 (paragraphs [0579]–[0590]), which explicitly describes classifier 100000252 as having the format "*SCORE = –1.839 + 0.8*HSP90AA1 – 1.5525*IKBKAP + 1.10184*IL13RA1 – 0.78923*LAMC1 – 1.3974*MAFB + 1.0602*PF4*". Additionally, paragraph [0249] of the published application teaches, using as an example the general form of a multiple regression equation of which classifier 100000252 is a specific instance, that the terms HSP90AA1, IKBKAP, IL13RA1, LAMC1, MAFB and PF4 of classifier 100000252 are variables corresponding to measured data values for molecular markers, *i.e.*, expression levels. It would have been understood that the term "–1.839" in classifier 100000252 represents the sum of the two constants α and ε of the general form of a multiple regression equation taught at paragraph [0249] of the published application.

Thus, the claim amendments are fully supported by the specification and do not introduce new matter. Upon entry of this amendment, claims 76 and 82 to 98 will be pending.

Applicants note that an Information Disclosure Statement and revised PTO-1449 form were filed on February 9, 2010. However, the Office Action mailed May 11, 2010 does not include a signed off copy of the revised PTO-1449. Applicants respectfully request that the examiner consider the references listed on the PTO-1449 filed on February 9, 2010 and enter them into the record for this application.

The Rejections Under 35 U.S.C. § 112, Second Pararaph, Should Be Withdrawn

Claims 76 to 98 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In view of the amendments to independent claims 76, 87 and 93 and claims 83, 86, 89, 92, 95, and 98 and the remarks below, the rejections under 35 U.S.C. § 112, second paragraph, should be withdrawn.

First, the Examiner contends that it is unclear exactly what genes are represented by the acronyms HSPCA, IKBKAP, IL13RA1, LAMC1, MAFB, and PF4 in claims 76, 87 and 93. The Examiner requests clarification via clearer claim language.

Applicants respectfully traverse the rejection. Nevertheless, in the interest of expediting issuance of the application, Applicants have amended claims 76, 87 and 93, from which claims 77–86, 88–92, and 94–98 depend, so as to replace the acronyms, as described in the following Table of gene acronym replacement amendments.

Table of gene acronym replacement amendments.

ACRONYM	REPLACEMENT AMENDMENT
HSPCA	heat shock protein 90kDa alpha (cytosolic), class A member 1 (HSP90AA1)
IKBKAP	inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase complex-associated protein (IKBKAP)
IL13RA1	interleukin 13 receptor, alpha 1 (IL13RA1)
LAMC1	laminin, gamma 1 (LAMC1)
MAFB	v-maf musculoaponeurotic fibrosarcoma oncogene homolog B (avian) (MAFB)
PF4	platelet factor 4 (PF4)

Second, the Examiner contends that it is unclear, in claims 83, 86, 89, 92, 95, and 98, if classifier 100000252 is intended to be defined by the embodiment disclosed in the specification or if classifier 100000252 includes other embodiments that are not defined. The Examiner requests clarification via clearer claim language.

Applicants respectfully traverse the rejection. Nevertheless, in the interest of expediting issuance of the application, Applicants have amended claims 83, 86, 89, 92, 95, and 98 to specify that the classifier has the format SCORE = –1.839 + 0.8*HSP90AA1 – 1.5525*IKBKAP + 1.10184*IL13RA1 + 0.78923*LAMC1 – 1.3974*MAFB + 1.0602*PF4. The amended claims further specify that SCORE, if positive, classifies the test subject into the class representing human subjects having mild osteoarthritis; SCORE, if negative, classifies the test subject into the class representing human subjects not having osteoarthritis; HSP90AA1 represents the level of expression of heat shock protein 90kDa alpha (cytosolic), class A member 1 (HSP90AA1) in the sample of the test subject; IKBKAP represents the level of expression of inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase complex-associated protein (IKBKAP) in the sample of the test subject; IL13RA1 represents the level of expression of interleukin 13 receptor, alpha 1 (IL13RA1) in the sample of the test subject; LAMC1 represents the level of expression of laminin, gamma 1 (LAMC1) in the sample of the test subject; MAFB represents the level of expression of v-maf musculoaponeurotic fibrosarcoma oncogene homolog B (MAFB) in the sample of the test

subject; and PF4 represents the level of expression of platelet factor 4 (PF4) in the sample of the test subject.

For the reasons discussed above, Applicants submit that the rejections under 35 U.S.C. § 112, second paragraph, have been overcome and the rejections should be withdrawn.

CONCLUSION

Applicants respectfully request that the above-made amendments and remarks be considered and entered into the application. The Examiner is invited to telephone the undersigned to discuss any questions concerning the application. An early allowance is earnestly sought.

Respectfully submitted,

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